

DEC 20 2006

Appl. No. 10/824,833
Amdt. dated December 20, 2006
Reply to Office Action of September 20, 2006

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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-51. (Cancelled)

52. A method of treating a viral infection in a mammal in need of such treatment, the method comprising administering a TLR ligand, and administering an IMPDH inhibitor.

53. The method of claim 52, wherein the IMPDH inhibitor is mizoribine, an enantiomer of mizoribine, mizoribine base, mizoribine aglycone, or a prodrug of such compound.

54. The method of claim 52, wherein the viral infection is caused by an RNA virus.

55. The method of claim 54, further comprising administering a synthetic TLR ligand.

56. The method of claim 54, wherein the viral infection is caused by an RNA virus selected from the group consisting of a coronavirus that causes Severe Acute Respiratory Syndrome (SARS) and a Hepatitis C Virus.

57. The method of claim 54, wherein the RNA virus is mutated and does not cause an induction of interferon synthesis.

58. The method of claim 54, wherein the IMPDH inhibitor is administered directly to the site of viral infection.

59. The method of claim 58, wherein the RNA virus is a coronavirus that causes SARS and the IMPDH inhibitor is administered to a lung.

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60. The method of claim 52, wherein the viral infection is caused by a DNA virus.

61. The method of claim 60, wherein the TLR ligand is a synthetic TLR ligand.

62. The method of claim 60, wherein the DNA virus is a Hepatitis B virus.

63. The method of claim 60, wherein the IMPDH inhibitor is given systemically.

64. A method for treating cancer comprising administering to a subject in need of such treatment a therapeutically effective amount of
(a) a member selected from an inhibitor of inosine monophosphate dehydrogenase (IMPDH), an enantiomer of such a compound, a prodrug of such a compound, a pharmaceutically acceptable salt of such a compound, and combinations thereof; and
(b) an interferon inducer.

65. The method of claim 64, wherein the cancer is an interferon-sensitive cancer.

66. The method of claim 65, wherein the interferon-sensitive cancer is a member selected from a leukemia, a lymphoma, a myeloma, a melanoma, and a renal cancer.

67. The method of claim 64, wherein the IMPDH inhibitor is selected from the group consisting of mizoribine, mizoribine base, mizoribine aglycone, mycophenolic acid, mycophenolate mofetil, Tiazofurin and ribavirin.

68. The method of claim 64, further comprising administration of therapeutically effective amount of a Type I interferon.

69. The method of claim 64, wherein the interferon inducer comprises a therapeutically effective amount of a pharmaceutical composition, wherein the pharmaceutical

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composition comprises a nucleic acid of claim 14, wherein the nucleic acid comprises a toll-like receptor (TLR) ligand.

70. The method of claim 69, wherein the TLR ligand binds to a TLR expressed on an endosomal membrane.

71. The method of claim 69, wherein the composition further comprises a CpG oligonucleotide (ISS-ODN).

72. The method of claim 69, wherein the composition is administered to a mucus membrane.

73. The method of claim 69, wherein the TLR ligand is a homofunctional TLR ligand polymer.

74. The method of claim 73, wherein the homofunctional TLR ligand polymer comprises a TLR ligand selected from the group consisting of a TLR-7 ligand and a TLR-8 ligand.

75. The method of claim 74, wherein said homofunctional TLR ligand polymer comprises a TLR-7 ligand.

76. The method of claim 75, wherein said TLR-7 ligand is a member selected from the group consisting of a 7-thia-8-oxoguanosinyl (TOG) moiety, a 7-deazaguanosinyl (7DG) moiety, and an imiquimod moiety.

77. The method of claim 74, wherein the homofunctional TLR ligand polymer comprises a TLR-8 ligand.

78. The method of claim 77, wherein the TLR-8 ligand is a resiquimod moiety.

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79. The method of claim 69, wherein said TLR ligand is a heterofunctional TLR ligand polymer.

80. The method of claim 79, wherein said heterofunctional TLR ligand polymer comprises a TLR-7 ligand and a member selected from the group consisting of a TLR-8 ligand and a TLR-9 ligand.

81. The method of claim 79, wherein said heterofunctional TLR ligand polymer comprises a TLR-7 ligand, a TLR-8 ligand, and a TLR-9 ligand.

82. The method of claim 79, wherein said heterofunctional TLR ligand polymer comprises a TLR-8 ligand and a TLR-9 ligand.

83. A method for treating an autoimmune disease comprising administering to a subject in need of such treatment a therapeutically effective amount of

(a) a member selected from an inhibitor of inosine monophosphate dehydrogenase (IMPDH), an enantiomer of such a compound, a prodrug of such a compound, a pharmaceutically acceptable salt of such a compound, and combinations thereof; and

(b) an interferon inducer.

84. The method of claim 83, wherein the IMPDH inhibitor is selected from the group consisting of mizoribine, mizoribine base, mizoribine aglycone, mycophenolic acid, mycophenolate mofetil, Tiazofurin and ribavirin.

85. The method of claim 83, wherein the autoimmune disease is multiple sclerosis.

86. The method of claim 83, further comprising administering a therapeutically effective amount of a Type I interferon.

87. The method of claim 83, wherein the interferon inducer comprises a therapeutically effective amount of a pharmaceutical composition, wherein the pharmaceutical

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composition comprises a nucleic acid of claim 14, wherein the nucleic acid comprises a toll-like receptor (TLR) ligand.

88. The method of claim 87, wherein the TLR ligand binds to a TLR expressed on an endosomal membrane.

89. The method of claim 87, wherein the composition further comprises a CpG oligonucleotide (ISS-ODN).

90. The method of claim 87, wherein the composition is administered to a mucus membrane.

91. The method of claim 87, wherein said TLR ligand is a homofunctional TLR ligand polymer.

92. The method of claim 91, wherein the homofunctional TLR ligand polymer comprises a TLR ligand selected from the group consisting of a TLR-7 ligand and a TLR-8 ligand.

93. The method of claim 92, wherein said homofunctional TLR ligand polymer comprises a TLR-7 ligand.

94. The method of claim 93, wherein said TLR-7 ligand is a member selected from the group consisting of a 7-thia-8-oxoguanosinyl (TOG) moiety, a 7-deazaguanosinyl (TDG) moiety, and an imiquimod moiety.

95. The method of claim 92, wherein the homofunctional TLR ligand polymer comprises a TLR-8 ligand.

96. The method of claim 95, wherein the TLR-8 ligand is a resiquimod moiety.

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97. The method of claim 87, wherein said TLR ligand is a heterofunctional TLR ligand polymer.

98. The method of claim 97, wherein said heterofunctional TLR ligand polymer comprises a TLR-7 ligand and a member selected from the group consisting of a TLR-8 ligand and a TLR-9 ligand.

99. The method of claim 97, wherein said heterofunctional TLR ligand polymer comprises a TLR-7 ligand, a TLR-8 ligand, and a TLR-9 ligand.

100. The method of claim 97, wherein said heterofunctional TLR ligand polymer comprises a TLR-8 ligand and a TLR-9 ligand.

101. A method of treating a disease accessible to topical treatment in a subject in need of such treatment comprising administering a therapeutically effective amount of an interferon inducer, wherein said interferon inducer is given topically or delivered directly to a diseased tissue; and

administering a therapeutically effective amount of a member selected from an inhibitor of inosine monophosphate dehydrogenase (IMPDH), an enantiomer of such a compound, a prodrug of such a compound, a pharmaceutically acceptable salt of such a compound, and combinations thereof.

102. The method of claim 101, wherein the interferon inducer is a TLR ligand.

103. The method of claim 102, wherein the TLR ligand is selected from the group consisting of resiquimod, imiquimod, and ISS-ODN.

104. The method of claim 102, wherein the TLR ligand is a nucleic acid of claim 14.

105. The method of claim 101, wherein the IMPDH inhibitor is administered systemically.

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106. The method of claim 101, wherein the IMPDH inhibitor is a member selected from the group consisting of mizoribine, mizoribine base, and mizoribine aglycone.

107. The method of claim 101, wherein the disease accessible to topical treatment is selected from the group consisting of cancer and precancerous conditions.

108. The method of claim 107, wherein the cancer is selected from the group consisting of melanoma, superficial bladder cancer, actinic keratoses, intraepithelial neoplasia, and basal cell skin carcinoma.

109. The method of claim 107, wherein the precancerous condition is selected from the group consisting of actinic keratoses and intraepithelial neoplasia.

110. The method of claim 101, wherein the disease accessible to topical treatment is a viral disease.

111. The method of claim 110, wherein the viral disease is a selected from the group consisting of a human papilloma virus infection, a molluscum contagiosum, and a herpes virus infection.

112. A method of treating cancer in a subject in need of such treatment comprising administering a therapeutically effective amount of a member selected from mizoribine, mizoribine base, mizoribine aglycone, an enantiomer of such a compound, a prodrug of such a compound, a pharmaceutically acceptable salt of such a compound, and combinations thereof; in combination with a therapeutically effective amount of Type I interferon.

113. The method of claim 112, wherein the cancer is a member selected from a leukemia, a lymphoma, a myeloma, a melanoma, and a renal cancer.

114. A method of treating a viral infection in a subject in need of such treatment comprising administering a therapeutically effective amount of a member selected from mizoribine, mizoribine base, mizoribine aglycone, an enantiomer of such a compound, a

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prodrug of such a compound, a pharmaceutically acceptable salt of such a compound, and combinations thereof; in combination with a therapeutically effective amount of Type I interferon.

115. The method of claim 114, wherein the viral infection is caused by a virus selected from the group consisting of a coronavirus that causes Severe Acute Respiratory Syndrome (SARS), a Hepatitis B virus, and a Hepatitis C Virus.

116. A method of treating an autoimmune disease in a subject in need of such treatment comprising administering a therapeutically effective amount of a member selected from mizoribine, mizoribine base, mizoribine aglycone, an enantiomer of such a compound, a prodrug of such a compound, a pharmaceutically acceptable salt of such a compound, and combinations thereof; in combination with a therapeutically effective amount of Type I interferon.

117. The method of claim 116, wherein the autoimmune disease is Multiple Sclerosis.

118. A method of treating Crohn's Disease in a subject in need of such treatment comprising administering a member selected from an inhibitor of inosine monophosphate dehydrogenase (IMPDH), an enantiomer of such a compound, a prodrug of such a compound, a pharmaceutically acceptable salt of such a compound, and combinations thereof; and a member selected from the group consisting of probiotics and glycolipids.